Conferences and Reviews

Melanoma Risk Factors and Atypical Moles

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Despite important advances in the treatment of melanoma, the prognosis for advanced disease remains discouraging. This fact, in combination with a worldwide epidemic of melanoma among persons of white skin type, has focused attention on identifying melanoma in its early, surgically curable stages. Attention has also been directed toward pinpointing which persons are at increased risk for melanoma to reduce risk where possible and to aid early diagnosis. Essentially all epidemiologic studies have identified an increased number of melanocytic nevi as an important risk factor in the development of melanoma, but controversy has arisen concerning the risk associated with certain types of nevi, particularly "dysplastic" nevi. We review melanoma risk factors and examine the relationship between melanocytic nevi and melanoma to clarify for primary care physicians what is "known" (noncontroversial) and what is "unknown" (controversial). We propose a working definition of an atypical mole phenotype and outline an approach to managing high-risk patients.

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An increased incidence of malignant melanoma is easily documented from various areas of the world.[1-3] Melanoma has been of interest to epidemiologists, pathologists, and clinicians in this regard for many years. Incidence rates have doubled each decade for the past two decades.[2] The death rate has also increased, but at a much lower rate—about 5% per year.[2] A decade ago the most rapid increase in the incidence of melanoma occurred in the lower legs of women in the 40- to 60-year age groups. Currently the most rapid increase in incidence is occurring in older persons, primarily older men, in the head and neck regions.[4] The increased incidence of melanoma has been attributed in part to earlier diagnosis because the five-year survival of melanoma patients has dramatically improved. For example, in 1960 the five-year survival of patients with malignant melanoma was 40%; in 1990 it was 83%.[2] The increase in incidence and survival cannot be attributed to either a change in diagnostic criteria or to a change in disease definition[3]; it appears to be a real event.

Melanoma is also of interest because it begins on the surface of the skin, is commonly associated with melanocytic nevi (moles), and is usually pigmented. The observation of precursor and early lesions affords the opportunity to interrupt tumor progression at a curable stage of evolution. As many as 80% of patients with melanoma report a change in a preexisting mole.[5] Yet, considerable controversy has surrounded the frequency with which melanomas are histologically associated with melanocytic nevi.[5-7] Whereas in most studies only a third of melanomas arise contiguous with benign nevi, several factors may affect these estimates, including tumor thickness (larger tumors may obliterate the preexisting nevus) and whether the entire lesion is examined stepwise. A recent review of the University of California, San Francisco, Melanoma Clinic data base revealed that more than 50% of primary melanomas arose in histologic association with a precursor nevus.[8] Furthermore, when only thin tumors were analyzed—less than 1.5 mm in tumor thickness—where the likelihood of obliteration would be less, 64% of primary melanomas were associated with precursor nevi.

Risk Factors for Melanoma

Differentiating persons at increased risk for melanoma and identifying the factors that underlie that risk should both enhance the diagnosis of early melanoma through close surveillance of high-risk persons and point to opportunities for reducing risk. Several studies have identified melanoma risk factors by comparing melanoma patients with control groups, from which composite relative risk tables have been constructed (Table 1).[1,9-22] The relationship between acquired nevi, both common and "dysplastic" (atypical) types, and the development of malignant melanoma is the primary subject of this review. Appropriate management of at-risk patients, however, requires an overall assessment of their melanoma risk factors.

The predominance of lightly pigmented persons in the melanoma population, as determined by skin, eye, hair

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TABLE 1.—*Melanoma Risk Factors*†*

Factor	Estimated Relative Risk
Changing pigmented lesion	Very high
Xeroderma pigmentosum	500
FAMM syndrome kindred	
Previous melanoma	500
Atypical nevi but no previous melanoma	150
Numerous common nevi	5-65
Atypical nevi	7-20
Giant congenital nevus	5-15
Previous melanoma	9
Lentigo maligna	5-10
Immunosuppression	4-7
Sun sensitivity	2-3
Excessive sun exposures	2-4
Melanoma in first-degree relative	2-12
Few or no common nevi	0.3
Hispanic or African-American persons	0.08-0.15
Age <15 years	0.01

FAMM = familial atypical mole or melanoma

*Average risk = 1.

†Estimates are derived from Koh[1] and Rhodes et al[9] and modified by data from Roush et al,[10] Evans et al,[11] Kraemer et al,[12] Greene et al,[13] Weinstock and Sober,[14] Greene et al,[15] Nordlund et al,[16] Halpern et al,[17] Garbe et al,[18] Rhodes et al,[19] Quaba and Wallace,[20] and Kaplan.[21]

color, or a history of sun sensitivity, is striking.[23,24] In contrast, persons of more darkly pigmented races have a low incidence of melanoma, and in them melanomas predominate on unusual sites, such as palms or soles and mucous membranes.[25] An association between melanoma and excessive exposure to sun or cutaneous signs of chronic actinic damage has been repeatedly noted.[11,26,27] The predominant sites of melanoma, however, are those exposed to intermittent, intense sunlight, such as the back (men) and legs (women), and not those receiving more constant exposure, such as the face and dorsal hands and forearms, that are favored by the epithelial malignant tumors, squamous and basal cell carcinomas.[26,28] Similarly, several epidemiologic studies have linked brief intense sun exposures, such as severe sunburns, especially during childhood or in relation to sun vacations, to increased melanoma risk.[27,29-32] Indeed, the increased incidence of melanoma associated with higher socioeconomic status or educational level[29,33,34] may derive in part from the penchant of the affluent for sun vacations.[11] Finally, patients with xeroderma pigmentosum, an autosomal recessive trait of impaired DNA repair to ultraviolet light injury, have a high risk of melanoma.[12]

Immunosuppression, including human immunodeficiency virus infection, has also been linked to an increased incidence of melanoma.[13,35] Moreover, melanomas may be more aggressive in these patients.[13]

The remainder of the known melanoma risk factors listed in Table 1 relate to melanocytic nevi. Large congenital melanocytic nevi—nevi greater than 9 cm in diameter—are uncommon, occurring in less than 1 in 20,000 births,[36] but carry a substantial lifetime risk for melanoma (relative risk, 5 to 15).[37-39] The management of these patients is complex due to the size and extent of their lesions and the propensity for melanoma to develop during childhood and at unusual sites, such as the central nervous system.[40,41] The melanoma risk associated with more common (occurring in about 1% of newborns), small congenital nevi is controversial,[37] due to the absence of reliable criteria to distinguish them from other nevi in adults.[42,43] At present it may be prudent to consider removing small congenital nevi if their clinical features are such that early detection of melanoma would be difficult—for example, very dark or variable color and topography or difficult-to-observe site—and if the patient has other melanoma risk factors.

Lentigo maligna macules carry a 5% to 10% risk for the development of an invasive melanoma.[14] They are recognized clinically as an expanding, irregularly pigmented macule in middle-aged and elderly adults with ongoing exposure to sun and histopathologically by the proliferation of atypical melanocytes within the basal epidermal layer.

Acquired Nevi and Melanoma Risk

A major risk factor for melanoma in virtually every study has been the presence of numerous acquired melanocytic nevi, although the magnitude of the estimated risk varies considerably between studies.[11]* In general, the higher the nevus counts, the higher the risk. Moreover, several studies noted increasing risk in relation to increments of nevus numbers (Table 2).[32,44-49] Taken together, these and other studies indicate that melanoma risk is roughly proportionate to the number of melanocytic nevi.

Thus, although it is well established that high mole counts characterize persons at increased risk for melanoma, the nature of the relationship is controversial. There is disagreement about the percentage of melanomas that appear to arise from preexisting nevi histopathologically, with estimates ranging from about 20% to as high as 64% for thin melanomas (discussed earlier). Because the age distribution of acquired nevi and melanoma differs—that is, nevus counts decline after age 50,[50,51] whereas the incidence of melanoma continues to rise with advancing age—this might further suggest that they are unlikely to be histogenetically related. The proliferation of melanocytes at the dermoepidermal junction (junctional activity) is more common in the moles of younger people, whereas moles in older people atrophy and ultimately disappear. On the other hand, older patients with melanoma have junctional proliferation associated with their melanomas, and the "activation" of nevi in the region of the primary melanoma has been noted.[52] Thus it is possible that patients in whom melanomas develop have abnormally persistent junctional activity in their moles. Junctional proliferation in clinically atypical (dysplastic) nevi is known to persist in later life.[52]

Body sites with higher mole counts are preferential sites for the development of melanoma.[46,53] Both melanomas and nevi of either the common or dysplastic types

*See also the editorial by R. L. Barnhill, MD, "Moles and Melanoma—New Method in the Madness," on pages 381-384 of this issue.

TABLE 2.—*Relative Risk of Melanoma in Relation to Number of Benign Nevi*

Study	Country	Nevus Definition	Nevus Counts	Relative Risk
Holly et al, 1987[44]	United States	≥2 mm, whole body "nondysplastic"	11-25	1.6
			26-50	4.4
			51-100	5.4
			>100	9.8
Weiss et al, 1991[45]	Germany	"Benign" nevi	10-50	4.3
			>50	14.9
Krüger et al, 1992[46]	Germany	≥2 mm, trunk (men)	5-10	2.9
			11-20	5.5
			>20	32.6
			>40	133.4
Swerdlow and Green, 1987[47]	Scotland	≥2 mm, whole body	10-24	4.4
			25-49	8.7
			≥50	63.8
Green et al, 1985[48]	Australia	≥2 mm, left arm	2-4	15.7
			5-10	14.9
			>10	20.1

predominate on sites receiving intermittent, rather than constant, sun exposure, with the lowest numbers occurring on sun-shielded areas.[26,28,46,53-56] These observations suggest that even if melanomas do not invariably arise from preexisting nevi, both may arise through common stimuli, the most likely source according to epidemiologic studies being sunlight exposure. The strongest evidence for a relationship between sun exposure and melanocytic nevi derives from studies correlating the number of nevi with age at the time of immigration to sunny climates; higher mole counts were associated with immigration during childhood.[57,58] Occasional anecdotal accounts of nevi occurring in sites of previous severe sunburn provide further support for such a relationship (R.W.S., unpublished observations, August 1993).

Most studies also note higher mole counts in light-skinned persons.[54,56,57,59-61] Whether this relationship derives solely from the increased sun sensitivity of light-skinned persons or points to other genetically determined factors is unclear. Twin studies have provided strong evidence for a genetic factor(s) in determining nevus number, by demonstrating that mole counts are similar in identical, but not in fraternal, twins.[62] An increased number of melanocytic nevi are also reported in the chromosomal disorders Turner syndrome (XO)[63] and ring chromosome 7 syndrome.[64] Finally, an increased number of nevi has been reported in children following renal transplantation[65] or chemotherapy for a malignant tumor,[66,67] suggesting that immune function is an additional determinant of nevus numbers.

In summary, it appears that environmental (sun exposures), physiologic (immune function), and genetic factors determine the number of melanocytic nevi that will develop in a person. In view of the strong association between nevus number and melanoma risk, reducing sun exposures during childhood would be expected to substantially reduce this risk. Furthermore, children at increased risk for numerous moles—fair-skinned children or those with a family history of either melanoma or an abnormal mole phenotype (discussed later)—should benefit most from behavioral modification. Adults with numerous nevi should be examined for other melanoma risk factors, and observed appropriately (see later discussion).

Dysplastic Nevi

Origin of the Concept and Current Controversy

Moles with an unusual structure (Table 3) were first noted in families with a high incidence of melanoma. These were first reported as the "B-K mole syndrome" to acknowledge families "B" and "K"[68] and as the familial atypical mole and melanoma (FAMM) syndrome.[69] Shortly thereafter, these mole patterns were described in patients with and without melanoma who lacked a family history of melanoma, and the concept of the dysplastic nevus syndrome was expanded to include a "sporadic" dysplastic nevus syndrome for nonfamilial cases.[70] Controversy then began when the clinical definition was extended so that the presence of smaller lesions and fewer

TABLE 3.—*Clinical Features of Typical Nevi, Atypical Nevi, and Melanoma*

Clinical Feature	Common Nevi	Atypical Nevi	Melanoma
Size	Usually <5 mm	Varies, often >5 mm	Varies, may be >10-15 mm
Shape	Round; well-defined borders	Irregular; ill-defined borders	Irregular; notched borders
Color	Even	Variable; shades of brown; may be very dark regions; erythema often present	Variable; shades of brown to black; also red (inflammation), white (regression), and blue (pigment deep in dermis)

moles was being diagnosed as the dysplastic nevus syndrome. About a third of patients in a referral melanoma clinic were found to have clinically dysplastic nevi,[70] whereas the prevalence of dysplastic nevi in the general population reported over the next few years ranged from 4.9%[71] to 49%.[72]

At the same time, controversy also grew over the histopathologic correlation with these atypical nevi. Both architectural changes—lateral extension of the junctional component beyond the central nevus, complex lentiginous elongation of the epidermal ridge pattern, and fibroplasia of the papillary dermis—and cytologically noted atypia were included in the original definition. These changes also occur along a spectrum, and controversy similarly arose about the defining limits. Some pathologists required microscopic evidence of atypia of melanocytes in their definition of dysplasia.[73,74] In a review of early and nonfamilial cases, dysplastic nevi were divided histologically into low-grade and severe, based primarily on the degree of atypia of the junctional melanocytes.[75] Other authors accepted either architectural or cytologic changes.[72] Conversely, one author has categorically rejected both the clinical and histologic spectrums of dysplastic nevi on the grounds that dysplastic nevi should be considered merely melanocytic nevi of a flat and common type.[76] At the most recent National Institutes of Health consensus conference on the subject,[3] it was recommended that the clinical term "atypical nevus" be substituted for "dysplastic nevus" and that a more cumbersome description of architectural changes and cytologic atypia for the histologic dysplastic lesion be adopted. Nonetheless, the biologic concept of melanocytic dysplasia is useful in understanding the spectrum of tumor progression.[77]

Familial Atypical Mole or Melanoma Syndrome

Despite the foregoing controversy concerning the definition of melanocytic dysplasia, the existence of a syndrome of familial melanoma, defined as kindreds having two or more first-degree relatives with melanoma and in which nearly all affected persons have an unusual mole pattern that is characterized by an increased number of clinically atypical nevi (see Table 3), is noncontroversial.[3] Variably called the familial atypical multiple mole or melanoma (FAMM) syndrome,[78] the familial dysplastic nevus syndrome, type D2,[79] or the B-K mole syndrome,[68] the disorder is inherited as an autosomal dominant trait with incomplete penetrance and variable expressivity.[15,78,80-82] Linkage studies have suggested a locus on chromosome 1p,[83] but this has been refuted in other kindreds.[82,84-86] More recently, linkage to a cancer-associated region was demonstrated on the short arm of chromosome 9.[87] Whether these differences in linkage analysis are due to the use in some studies of an ambiguous marker, the "dysplastic" nevus, rather than melanoma, as suggested by some authors,[84,87] or reflect genetic heterogeneity is unclear. The latter interpretation is favored by evidence of clinical heterogeneity, including familial melanoma kindreds without dysplastic nevi.[82,86] or with ocular melanoma or other malignant neoplasms.[88,89] Affected family members can be identified in childhood or adolescence by the appearance of multiple nevi having the clinical (see Table 3) or histopathologic features of atypical or dysplastic nevi. It has been estimated that affected persons in FAMM kindreds have a 100% risk of a melanoma developing by age 70.[15,79] Melanomas develop at an earlier age in FAMM kindreds than in the general public,[78] and survivors are at high risk for additional primary melanomas.[15] Close surveillance of these patients for the detection of early melanoma is clearly warranted.[3]

Melanoma Risk Associated With Atypical ('Dysplastic') Moles

Whereas the presence of atypical moles, characterized by irregularities of pigmentation and shape, often with hazy borders and large size (see Table 3), is a strong predictor of melanoma risk in familial melanoma kindreds,[15] the importance of atypical moles in the general public is controversial.[3] Nonetheless, several studies have shown an increased risk for melanoma associated with clinically defined atypical nevi (Table 4).[10,16-18,44,51] These studies compared mole phenotypes in a group of melanoma patients with those of an age- and usually sex-matched control (white) group. The precise definition of an atypical

TABLE 4.—*Melanoma Risk Associated With Clinically Defined 'Dysplastic' Nevi in Melanoma Patients versus Controls*

Study	Country	Definition	≥1 Dysplastic Nevi, %		Relative Risk
			Melanoma Patients	Controls	
Roush et al, 1986[10]; Nordlund et al, 1985[16]..	Australia	>5 mm, irregular border, and haphazard pigmentation	34	7	7.7
Mackie et al, 1985[51].....	Scotland	>5 mm and irregular borders, irregular pigmentation, or inflammation	38	20	2.1-4.5*
Holly et al, 1987[44]	United States	At least 3 of 6 criteria: ill-defined border, irregular border, irregular pigmentation, >5 mm, erythema, accentuated skin markings	55	17	3.8-6.3†
Halpern et al, 1991[17].....	United States	>4 mm, macular component, variegation of color, and irregular or indistinct border	39	7	8.8
Garbe et al, 1989[18].....	Germany	At least 3 of 5 criteria: >5 mm, irregular margins, ill-defined border, color variation, macular and papular components	45	5	7

*Relative risks for 1 or 2 atypical nevi: 2.1; for 3 or more atypical nevi: 4.5.
†Relative risks for 1 to 5 atypical nevi: 3.8; for 6 or more atypical nevi: 6.3.

nevus varied among the studies, which may account in part for the variation in estimated frequencies of atypical nevi in both control groups and patients. In all studies, estimated relative risks were adjusted for other known melanoma risk factors, such as total number of melanocytic nevi, skin type, and sun exposures. Some studies showed that a greater number of atypical nevi conferred a higher relative risk of melanoma,[16,44,51] whereas in others no increment in risk was observed.[17,18] Patients with dysplastic nevi had higher total mole counts in both melanoma patients and control groups than did persons without dysplastic nevi.[44] Moreover, patients with higher mole counts also had a greater number of atypical nevi.[44] Thus, although high numbers of moles and atypical moles are statistically independent risk factors for melanoma, they commonly occur in the same person. Hence, a strong correlation of melanoma risk with "nevus density" has been shown in which both the number and size of nevi are considered.[90]

The term "atypical mole syndrome" has been proposed to encompass the phenotype of an increased number of nevi (more than 100), some of which are large (>8 mm) and have atypical features.[91] Prospective follow-up of patients with this phenotype has shown a high risk for melanoma[92]; that is, over an average follow-up of four years, melanoma developed in 4.8% of these patients (in comparison with about a 1% risk of melanoma developing from ages 0 to 75 in the general population). The subset at greatest risk for melanoma comprised patients with the atypical mole syndrome and a previous melanoma. Although this study may reflect the bias of a referral center, a similarly high risk of melanoma associated with an abnormal mole phenotype was observed in a prospective study of nonreferred patients.[93]

Abnormal Mole Phenotypes and Melanoma Risk

The foregoing studies provide strong support for a clinically defined abnormal mole phenotype (Table 5) in which both the number of nevi and their quality (banal or atypical) are considered. Persons with an unquestionably abnormal mole phenotype form a relatively small fraction of the population and yet carry a greatly increased risk for melanoma.[93] Clearly a continuum of mole patterns exists from persons with few to no moles, to those with a moderate number (25 to 50) of nevi and some with possible to probable atypical features, to those with many moles (>50) and several to many that are clearly atypical.[93] It will be difficult, therefore, to rigidly define phenotypes and to defend these definitions.

TABLE 5.—*Mole Patterns*

Mole Feature	*Normal Mole Pattern*	*Abnormal Mole Phenotype*
Number.....	None to few (<25)	Many (>50)
Size.....	<5 mm	Variable: small to large, often several >5 mm
Color and shape ..	Uniform pigmentation, well circumscribed	Some to many nevi with irregular pigmentation, ill-defined borders, or erythema

TABLE 6.—*Follow-up of Patients With an Abnormal Mole Phenotype*

Mole Pattern	*Other Risk Factors*	*Nevus Photography*	*Follow-up Intervals, mo*
Abnormal.....	FAMM kindred: previous melanoma	Yes	3-4
Abnormal.....	FAMM kindred: no previous melanoma	Yes	4-6
Abnormal.....	Previous melanoma	Yes	4-6
Abnormal.....	Immunosuppressed	Yes	4-6
Abnormal.....	None	Yes*	12
Possibly abnormal..	Actinic damaged skin	Yes*	12
Normal.....	FAMM kindred: no previous melanoma	No	12

FAMM = familial atypical mole or melanoma

*If photography services are readily available.

The diagnosis of an abnormal mole pattern is one of gestalt, best achieved by standing back from the patient and taking in the whole picture. As a working definition, persons either with many nevi (>100) with or without atypical nevi, or with many nevi (>50) and with one or several clinically atypical nevi, should be considered to have an abnormal mole phenotype. Such patients should be examined closely for melanoma and any lesions suspicious for melanoma excised. The tendency to form atypical nevi, even outside FAMM kindreds, is familial.[94] First-degree relatives of patients with an abnormal mole phenotype should therefore be examined.[95,96]

To prescribe a plan for follow-up care, the presence of other known melanoma risk factors should be ascertained, particularly a personal or family history of melanoma, the presence of immunosuppression, and signs of pronounced sun sensitivity or excessive sun exposures (Table 6). Certain genetic disorders confer an exceedingly high risk for melanoma, such as xeroderma pigmentosum,[12] and members of FAMM kindreds who have already had one melanoma.[79] Close surveillance—every three to four months—of these patients is warranted. Members of FAMM kindreds with abnormal mole phenotypes in whom a melanoma has not yet developed should also be observed closely—every three to six months. Similar follow-up intervals are recommended for persons with an abnormal mole phenotype and either a previous melanoma or immunosuppression. Other patients with an abnormal mole phenotype may be observed annually. Because of the occasional discordance of atypical nevi and melanomas in FAMM kindreds,[15] adult members with a normal mole pattern should also be examined annually.

In general, we recommend excisional biopsy only of nevi whose clinical features are suspicious for melanoma (see Table 3). Often the melanoma will stand out from its neighbors in a field of common and atypical nevi as the "funniest" or "ugliest" mole (Figure 1). When patients are seen for the first time with numerous and varied atypical nevi, excisional biopsy of one or two of the most atypical

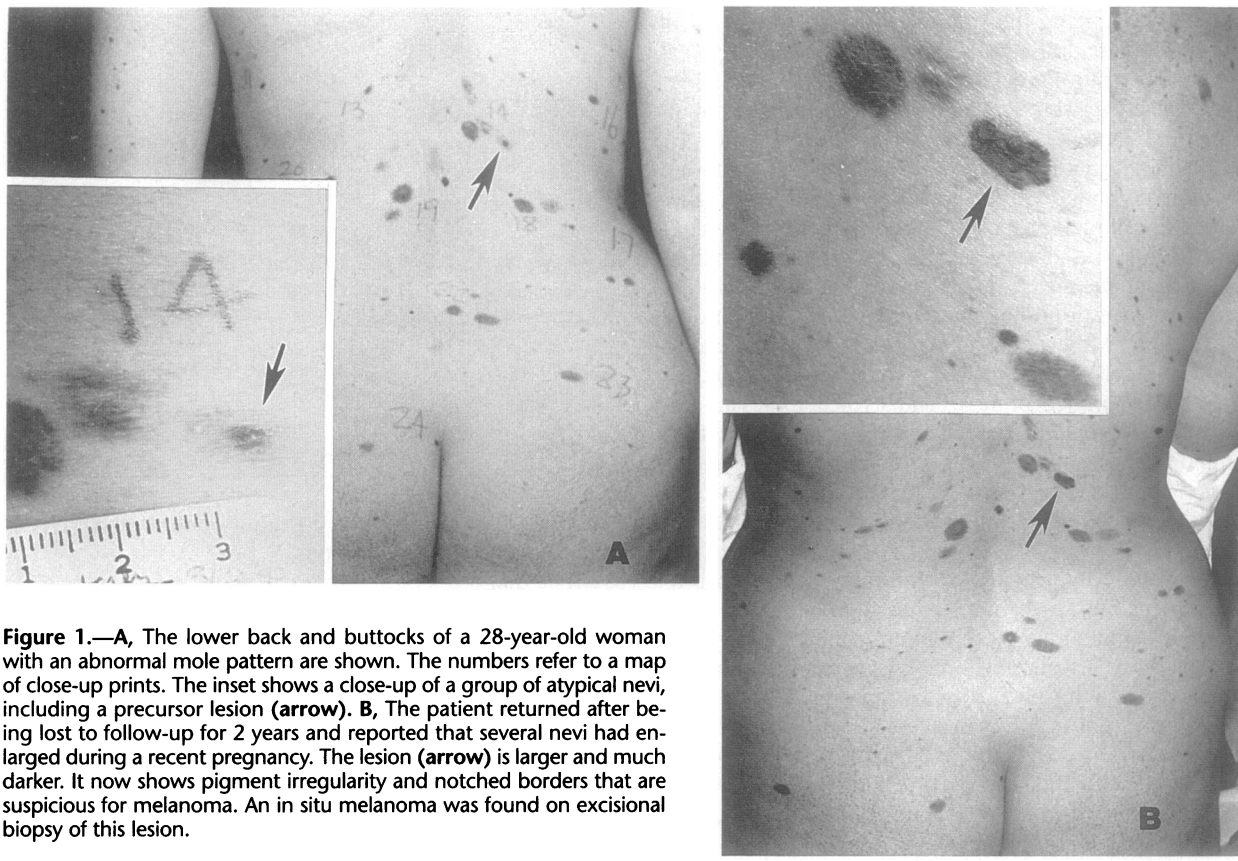

Figure 1.—A, The lower back and buttocks of a 28-year-old woman with an abnormal mole pattern are shown. The numbers refer to a map of close-up prints. The inset shows a close-up of a group of atypical nevi, including a precursor lesion **(arrow). B,** The patient returned after being lost to follow-up for 2 years and reported that several nevi had enlarged during a recent pregnancy. The lesion **(arrow)** is larger and much darker. It now shows pigment irregularity and notched borders that are suspicious for melanoma. An in situ melanoma was found on excisional biopsy of this lesion.

nevi to exclude early melanoma may be reasonable. New or changing pigmented lesions as a general rule should be removed, although there are reasonable exceptions. For example, new or enlarging nevi in adolescents and young adults (younger than 30 years) are common and need only be removed if they have suspicious features.

The role of photographic documentation in observing patients with atypical nevi has been controversial.[97,98] The major obstacle to recommending universal implementation of nevus photography in the follow-up of high-risk patients is the limited availability of services providing high-quality, standardized views. We and others have found photographs useful in observing adults with an abnormal mole phenotype (see Figure 1).[15,99,100] Their usefulness in detecting early melanomas in high-risk patients has been demonstrated by the New York University Skin and Cancer Unit.[92,101] In their experience, 60% of melanomas were detected solely on the basis of a change in the photographic record. Moreover, about 60% of malignant neoplasms arose de novo, that is, they were not associated histopathologically with a preexisting nevus. This implies that removing all clinically atypical nevi is not warranted even in high-risk patients because, in addition to the impracticality of removing what are often many lesions, such efforts will not eliminate risk. It may be prudent, however, to consider removing nevi in locations that are difficult to photograph and observe, such as the scalp, in high-risk persons, such as affected members of FAMM kindreds.[102] In the future, newer technologies, including epiluminescence microscopy (dermatoscopy) and digitalized images, may facilitate the follow-up of high-risk patients.[103,104]

Summary and Conclusions

In this review we have examined the factors that predispose persons to the development of melanoma, emphasizing the relationship between melanocytic nevi (moles) and melanoma risk. An understanding of the evolution of nevi in patients of different ages and the risks of melanoma associated with nevi of different types will be important to primary care physicians when addressing the concerns of their patients. Patients at varying degrees of risk may express concerns about their nevi. Some may have had family members or friends with melanoma, perhaps with a rapidly fatal outcome, and they may worry about either specific moles or their moles in general. Parents worry about their children, and spouses worry about each other. In our experience, many patients are reassured by our counseling, as most have imagined the risk of melanoma to be greater than we have counseled. In a recent study of the relative frequency of diagnoses in pigmented lesions removed and sent to a group of pathology laboratories,[105] of almost 3,000 consecutive examinations, 71% were benign nevi, 22% were diagnosed as "dysplastic," and preinvasive or invasive melanoma each accounted for less than 1% of such lesions. These data can help to reassure patients who are having biopsies done or who have moles that are being observed. These figures also suggest

that physicians are removing a high percentage of benign nevi in an attempt to diagnose early melanoma.

In most instances, follow-up of high-risk patients by physicians thoroughly trained in the diagnosis of pigmented lesions, such as dermatologists, is indicated (see Table 6). But the recognition of abnormal mole patterns for appropriate patient referrals is an important task for primary care physicians. In addition, all physicians should be familiar with the clinical signs of melanoma[1,80,106] to facilitate the early diagnosis and treatment of these epidemic cancers in their patients and family members. In this time of change in the health care system, the responsibility for the initial recognition of early melanoma will increasingly fall on primary care physicians. Our intent with this review is to provide some of the background information required in this role.

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